Clinical Summary: Intra-arterial Pressure-Enabled Drug Delivery™ Significantly Increases Penetration of Glass Microspheres in a Porcine Liver Tumor Model

Jaroch DB, Liu Y, Kim AY, Katz SC, Cox BF, Hullinger TG, Intra-arterial Pressure Enabled Drug Delivery Significantly Increases Penetration of Glass Microspheres in a Porcine Liver Tumor Model, Journal of Vascular and Interventional Radiology (2024), doi: https://doi.org/10.1016/ j.jvir.2024.06.030.

SUMMARY:

A preclinical study in transgenic pigs (Oncopigs) with induced liver tumors demonstrated that Pressure-Enabled Drug Delivery (PEDD™) with a TriNav Infusion System significantly improved the tumor uptake of glass microspheres (GM) compared to a traditional microcatheter (MC).

The study involved both lobar and selective infusions of fluorescently labeled GM to simulate TARE-Y90 therapy delivery. After the hepatic arterial infusions were completed, a specialized imaging tool was used to detect GM fluorescent signal in and around tumors, and a blinded quantitative analysis of signal intensity was performed with a custom deep learning algorithm.

TriNav with PEDD was shown to significantly improve GM uptake in liver tumors relative to a traditional MC in both lobar and selective infusions (n=17 each). The study showed that compared to a traditional MC:

- In lobar infusions TriNav increased tumor penetration by 117% (p=0.004)
- In selective infusions TriNav increased tumor penetration by 39% (p=0.032)
- Lobar infusions using a TriNav had tumor penetration that was statistically equivalent to selective delivery using a traditional MC (p=0.497)

The results of this study are clinically important for demonstrating how TriNav can improve the tumor penetration of GM.

STUDY DESIGN:

This study was designed to test the hypothesis that using a TriNav would improve the delivery of glass microspheres into and around a tumor compared to a traditional MC in both selective and lobar hepatic arterial infusions.

Oncopigs have genetic mutations which facilitate the development of cancerous, hypovascular, tumors. In this study, Oncopigs had tumors induced which were allowed to grow for 8-10 days, and measured 1-3cm at the time of the experiments.

A fluorescently labeled silica glass microsphere was produced and delivered via hepatic arterial infusion to simulate TARE-Y90 therapy delivery. Infusions of GM were classified as either lobar or selective **(Figure 1)** and grouped by delivery method (PEDD using the TriNav or traditional MC). Tumor diameters and liver volumes were statistically equivalent in both the PEDD and traditional MC groups. All infusions were done using a TheraSphere™ Administration Set to deliver a 6 GBq equivalent dose of GM (2,400,000 spheres).

Livers were collected immediately after dosing, and serial 1cm thick cross sections were prepared. Near-Infrared (NearIR) imaging with a Pearl Trilogy Imaging System was performed to identify patterns of therapeutic uptake. Then a custom deep learning image analysis algorithm (Visiopharm A/S) was used to quantify the signal intensity in the tumors and surrounding tissue. The analysis portion of the study was blinded to what devices was used to deliver the GM (TriNav or traditional MC).

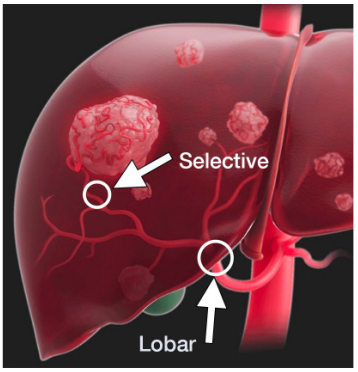

Figure 1. *Lobar vs selective artery placement. Lobar infusions were done in 2.0-3.5mm diameter vessels feeding 1 to 2 hepatic lobes. Selective infusions were done in 2nd or 3rd order vessels measuring 1.5-2.5mm in diameter and feeding ¼ to ½ of a targeted lobe.*

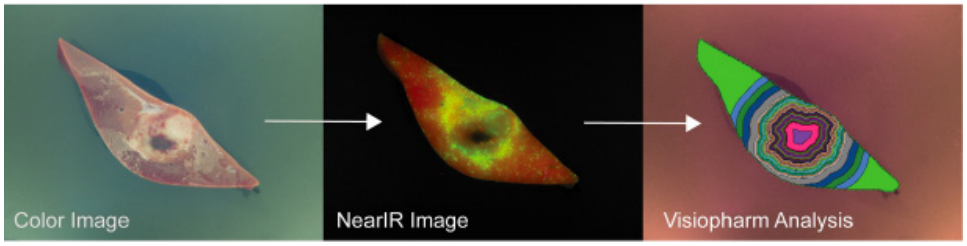

Figure 2. *Image analysis process example. A color image of the liver section is overlayed on the NearIR image showing GM distribution. The Visiopharm analysis then identifies the tumor border and generates concentric ROIs away from its edge to quantify GM distribution relative to the tumor.*

RESULTS:

The results of this preclinical study demonstrate that **hepatic arterial infusions via a TriNav significantly improved the tumor uptake of glass microspheres compared to a traditional microcatheter.** The blinded analysis showed that statistically significant increases in GM signal intensity were observed in each concentric zone from -20 mm into the tumor to 10mm away from the edge of tumor with PEDD compared to a traditional MC in both the lobar and selective delivery ($p \leq 0.05$).

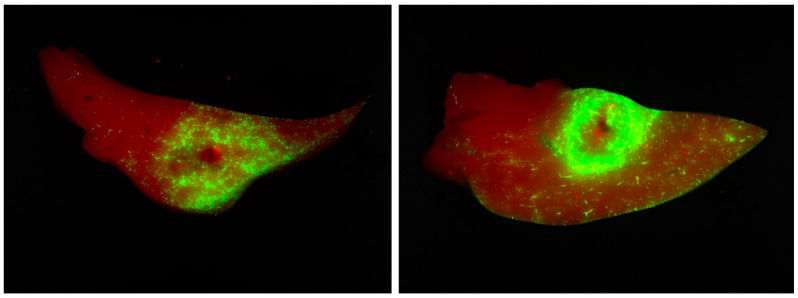

Figure 3. *Representative NearIR images of subjects treated with lobar delivery of GM via traditional MC (left) and via PEDD (right).*

The total penetration of GM, defined as the sum of signal intensity from -20mm to -1mm, was also analyzed. **For lobar delivery the total tumor penetration of GM was increased 117% with PEDD vs a traditional MC (p=0.004). For selective delivery the total tumor penetration of GM was increased by 39% (p=0.032).** (Figures 4a, 4b)

Of note, was that **lobar delivery using a TriNav had tumor penetration that was statistically equivalent to selective delivery using a traditional MC (p=0.497)**, which suggests that proximal infusions using a TriNav may enable effective delivery without selection of distal target vessels. **(Figure 4c)**

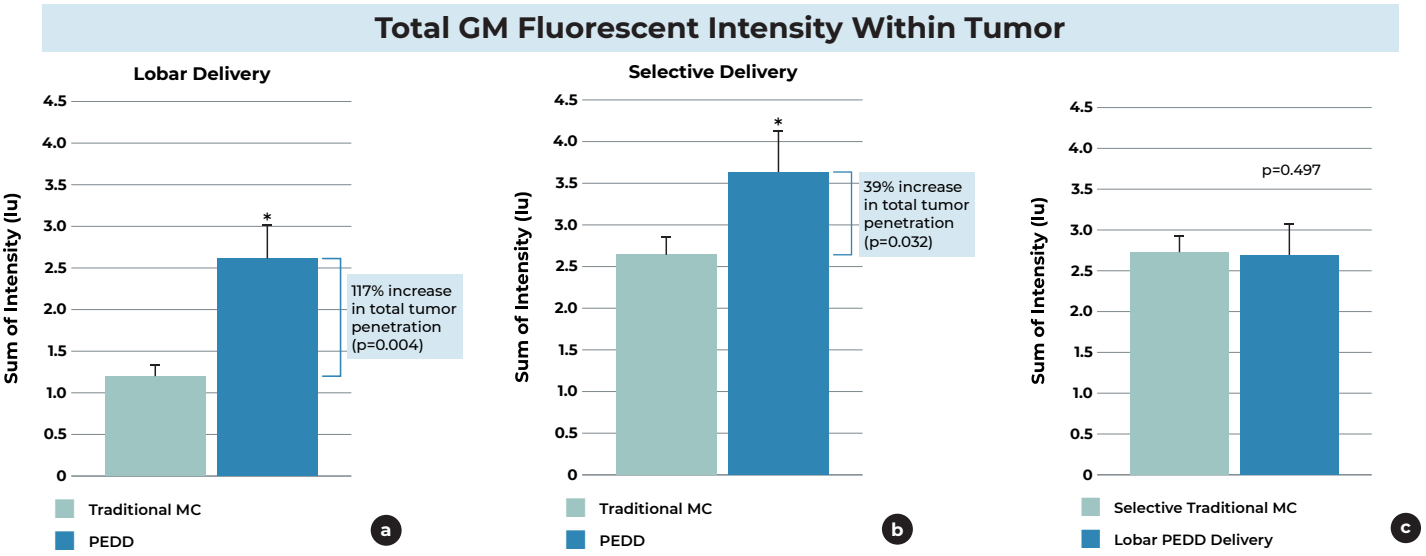

Figure 4. *Total tumor penetration of GM in (a) lobar delivery via PEDD vs traditional MC; (b) selective delivery via PEDD vs traditional MC; and (c) lobar delivery via PEDD compared to selective delivery via traditional MC.*

CONCLUSION:

This study demonstrated that using a TriNav device with the PEDD approach significantly improved delivery of GM, with greater delivery into porcine liver tumors in both proximal and selective infusions. Importantly, lobar PEDD infusions resulted in GM delivery equivalent to that achieved with the selective infusions with a traditional MC. The potential to selectively target multiple intrahepatic tumors from a single proximal location in the hepatic arterial system may expand the eligible patient population for TARE treatment.

The results observed in this study are congruent with prior clinical studies of primary and metastatic liver tumor patients treated with PEDD[1,2,3] and further demonstrate how PEDD has the potential to improve patient outcomes in TARE procedures.

1. Titano, J. J. et al. End-hole Versus Microvalve Infusion Catheters in Patients Undergoing Drug-Eluting Microspheres-TACE for Solitary Hepatocellular Carcinoma Tumors: A Retrospective Analysis. *Cardiovasc. Intervent. Radiol.* 42, 560–568 (2019).
2. Pasciak, A. S., McElmurray, J. H., Bourgeois, A. C., Heidel, R. E. & Bradley, Y. C. The impact of an antireflux catheter on target volume particulate distribution in liver directed embolotherapy: a pilot study. *J. Vasc. Interv. Radiol.* JVIR 26, 660–669 (2015).
3. d'Abadie P, Walrand S, Goffette P, et al. Antireflux catheter improves tumor targeting in liver radioembolization with resin microspheres. *Diagn Interv Radiol* 2021; 27:768–773.

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Results are not predictive of outcomes in other cases.

INDICATIONS FOR USE: The TriNav Infusion System is intended for use in angiographic procedures. It delivers radiopaque media and therapeutic agents to selected sites in the peripheral vascular system.
CONTRAINDICATIONS: TriNav is not intended for use in the vasculature of the central nervous system (including the neurovasculature) or central circulatory system (including the coronary vasculature).
Rx ONLY. For the safe and proper use of the TriNav device, refer to the Instructions for Use.

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